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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/706,328 | 11/12/2003 | Alison Hannah | 072121-0366 | 6441 |

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| EXAMINER | |
|---|---|
| ANDERSON, JAMES D | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1614 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/706,328 | HANNAH ET AL. | |
| | Examiner | Art Unit | |
| | James D. Anderson | 1614 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *02 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-38 and 49-64* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-38 and 49-64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**CLAIMS 1-38 & 49-64 ARE PRESENTED FOR EXAMINATION**

Applicants' amendment filed 3/2/2007 has been received and entered into the application. Accordingly, claim 20 is amended. In light of the amendments, as well as the remarks of applicants at pages 14-23 of their amendment, the objection to the claim 51 and the rejections of the claims under 35 U.S.C. § 112, 1st and 2nd paragraphs, as set forth in the previous Office action dated 11/2/2006 are hereby *withdrawn*. Applicants' arguments are not persuasive with respect to the double patenting rejections of claims (see below). Rejections not reiterated from the previous Office Action are withdrawn.

Upon further consideration, a new ground of rejection (35 U.S.C. 112, 2nd Paragraph) is being made. In light of this new ground of rejection, this Office Action is **Non-Final**.

***Claim Rejections - 35 USC § 112 (2nd Paragraph)***

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-38 and 49-64 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims recite administration of the claimed compound to provide specified $C_{max}$ and AUC values of the compound in a patient's plasma or blood. The ranges recited are in the form of, "a $C_{max}$ of about 20 to 4000 ng/mL" (*e.g.*, Claim 1). It is not clear from this claim language whether "about" modifies only the lower limit (*e.g.*, 20 ng/mL) or both the lower *and* upper limit (*e.g.*, 20 ng/mL and 4000 ng/mL). As such, the metes and bounds of the patent protection sought

are not clear. Amending the claims to either delete the word "about" from the lower limit or add the word "about" so as to modify the upper limit would overcome this rejection (*e.g.*, "a $C_{max}$ of 20 to 4000 ng/mL" or "a $C_{max}$ of about 20 to about 4000 ng/mL").

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR § 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR § 3.73(b).

U.S. Patent No. 6,605,617

Applicants' arguments have been fully considered but they fail to persuade the Examiner of error in his determination that the instant claims are obvious over claim 30 of the '617 patent. Firstly, Applicants' argue that because claim 30 of the '617 patent does not disclose a method of treatment directed to providing the claimed ranges of $C_{max}$ or AUC, it cannot obviate the present claims. This is not persuasive because the modifier "about" prefixes the recited ranges of Cmax or AUC. As such, because the instant specification does not define to what extent "about" modifies the ranges, the administration of any amount of the claimed compound will *necessarily* result in a $C_{max}$ or AUC that falls within this range. Claim 30 of the '617 patent recites the administration of an "effective amount". Such an effective amount could reasonably include an amount effective to provide a Cmax or AUC as instantly claimed. The Examiner refers to the specification of the '617 for a definition of "effective amount". At column 60, lines 41-51, the patentees disclose that a "therapeutically effective" dose may vary depending on the route of administration and dosage form. The preferred formulation exhibits a high therapeutic index (dose ratio between toxic effects and therapeutic effects). As such, the patentees clearly envisage a wide range of doses being administered to a patient. Accordingly, claims 1, 9, 36 and dependent claims are deemed properly rejected. Similarly, because claim 30 of the '617 does not recite any particular administration regimens or doses, it is up to the skilled artisan to determine the appropriate regimen and doses. The optimization of administration regimens and doses is well within the purview of the artisan skilled in the treatment of diseases. As such, when the general conditions are disclosed (in this case, administration of a compound to a patient), the skilled artisan would have been highly motivated to adjust treatment schedule, administration

route, dose, etc. in order to safely and effectively treat a patient. Accordingly, claim 49 and its dependent claims are deemed properly rejected. With respect to claims 52, 53 and dependent claims, the claimed formulas are metabolites of the compounds recited in instant claim 1. As such, if the compound of claim 1 is administered to a patient, the metabolites will necessarily be present to some extent. Thus, it would have been *prima facie* obvious to one of ordinary skill in the art to directly administer a metabolite of the compounds disclosed in the '617 patent. Accordingly, claims 52, 53 and dependent claims are deemed properly rejected. The rejection is maintained and reiterated below.

Claims 1-38 and 49-64 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 30 of U.S. Patent No. 6,605,617. Although the conflicting claims are not identical, they are not patentably distinct from each other because claim 30 of the '617 recites a method of treating a patient in need of an inhibitor of VEGF receptor tyrosine kinase comprising administering a compound according to any one of claims 1, 8, 15 or 22. The genus of compounds recited in the claims of the '617 patent include the instantly claimed compound. Further, the specification of '617 specifically recites the claimed compound (col. 86, Example 109) and further states that the disclosed compounds can be used to inhibit tumor growth (col. 61, lines 11-14). Thus, it would have been *prima facie* obvious to use the compounds disclosed in the '617 patent, including the instantly claimed compound, in a method to treat a cancer expressing VEGF. Further, because claim 30 of '617 is so broad so as to include administration of any amount of the claimed compounds to treat a VEGF mediated disease (including tumors), the claim renders obvious the instantly claimed ranges of $C_{max}$, AUC, and plasma concentrations of the instantly claimed compound.

U.S. Non-Provisional Application No. 10/886,950

Claims 1-7, 9-12, 14, 25-30, 36-38, and 52-64 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 13, 16 and 17 of copending Application No. 10/886,950. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '950 application are drawn to the treatment of a patient in need of an inhibitor of a receptor tyrosine kinase (claim 13) and wherein the patient is a cancer patient (claim 17). The instant application is drawn to the treatment of cancer wherein the cancer cells express a receptor tyrosine kinase comprising administration of the same compound. The claims differ in that the instant claims recite specific limitations with respect to $C_{max}$ and AUC. However, these limitations are an inherent property of the claimed compound when administered to a subject. As such, practice of methods of the '950 application would naturally result in the $C_{max}$ and AUC ranges as recited in the instant claims (*i.e.* administering the same compound to a subject to treat cancer would inherently result in the instantly claimed $C_{max}$ and AUC ranges). It is noted that the claims of the '950 application are extremely broad, encompassing the administration of the claimed compound in any dose to treat cancer. Naturally, there is at least one dose encompassed by the '950 claims that will result in the $C_{max}$ and AUC ranges instantly claimed.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

U.S. Non-Provisional Application No. 11/342,257

Claims 1-14, 25-30, 36-38, and 52-64 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5, 7-8, 10-17, 19-20 and 22 of copending Application No. 11/342,257. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '257 application are drawn to the treatment of a subject having a metastasized tumor (*i.e.* cancer) and the claims of the instant application are drawn to the treatment of cancer wherein the cancer cells express a receptor tyrosine kinase. The conflicting claims both comprise administration of the same compound. The claims differ in that the instant claims recite specific limitations with respect to $C_{max}$ and AUC. However, these limitations are an inherent property of the claimed compound when administered to a subject. As such, practice of methods of the '257 application would naturally result in the $C_{max}$ and AUC ranges as recited in the instant claims (*i.e.* administering the same compound to a subject to treat cancer would inherently result in the instantly claimed $C_{max}$ and AUC ranges). It is noted that the claims of the '257 application do not recite a specific dose. As such, the claims read on the administration of any dose of the claimed compound to treat cancer. Naturally, there is at least one dose encompassed by the '257 claims that will result in the $C_{max}$ and AUC ranges instantly claimed.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James D. Anderson whose telephone number is 571-272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

James D. Anderson, Ph.D.
Patent Examiner
AU 1614

May 10, 2007

Phyllis Spivack 5/10/07

PHYLLIS SPIVACK
SPE EXAMINER